Early versus Delayed Initiation of Continuous Renal Replacement Therapy in Critically Ill Patients with Acute Kidney Injury

Abdel-Basset El-Shaarawy Abdel-Azeem, Walid Anwar Abdel-Mohsen,
Maha Abd El Moneim Behairy, Ibrahim Al-Sayed Ibrahim Omar
Internal Medicine and Nephrology Department, Faculty of Medicine - Ain Shams University
Corresponding author: Ibrahimst Namei Omar, email: ibr.omar@yahoo.com

ABSTRACT

Aim of the work this study aimed to evaluate the impact of early versus late initiation of continuous renal replacement therapy on clinical outcomes in critically ill patients with AKI. **Results** regarding our retrospective cohort study and after prolonged exhaustive analysis of all the related data, some variables were found to be significantly related to the outcome of these critical ICU patients. These variables were systolic BP, WBCs, albumin, magnesium, PTT and INR at the start of CRRT. Some patients with AKI were associated with sepsis; there was a little benefit of early CRRT, in terms of ICU mortality. This needs further clarification by larger and high-powered studies.

Conclusion finally, the decision for early or late CRRT, in patients with AKI, should be individualized according to the clinical and laboratory parameters of each patient. It should also include the opinion of senior nephrologists, experienced in management of AKI. The decision should be sensitively communicated to the patients and/or their relatives, explaining the actual role of CRRT in management of their critical disorder.

Keywords: kidney Injury, replacement therapy, CRRT.

INTRODUCTION

Acute Kidney injury (AKI) is a well-recognized complication of critical illness with a large effect on morbidity and mortality. AKI is a common condition among patients in the intensive care unit (ICU). Forty percent of ICU patients developed evidence of AKI. Five percent of ICU patients received acute renal replacement therapy (ARRT) [1]. Despite increased knowledge of the management of critically ill patients, mortality associated with AKI remains [2]. Although the need for RRT in patients with severe AKI and life threatening complications is unequivocal, the optimal timing of RRT initiation in patients with severe AKI without life threatening complications has not yet been defined [3]. Earlier initiation of RRT may produce benefits by avoiding hypervolemia, elimination of toxins, establishing acid-base homeostasis, and preventing other complications attributable to AKI. However, early initiation of RRT may unnecessarily expose some patients to potential harm because some patients were spontaneously recoverd renal function [4].

Delaying RRT initiation unlikely had any immediate benefit per se. However, a delay may allow time for the stabilization of a patient condition before RRT was initiated and might avoid the need for such support, which was not devoid of risk [5]. Current evidence suggested reduced mortality and better renal recovery with earlier RRT initiation [6].

However, two observational studies reported high survival rates among patients who did not receive RRT [7]. One study reported adverse outcomes in association with very early RRT in patients with sepsis [8]. CRRT is a dialysis modality used to treat critically ill, hospitalized patients in ICU who developed AKI. It differs significantly according to the mechanism of solute transport, the type of membrane and the type of vascular access. CRRT provided slower solute clearance per unit time as compared to intermittent therapies. But over 24 h or more it may even exceed clearances with intermittent hemodialysis. Solute removal with CRRT was achieved either by convection (hemofiltration), diffusion (hemodialysis), or a combination of both these methods (hemodiafiltration) [9].

SUBJECTS AND METHODS

This was a retrospective observational cohort study, including 100 adult patients, who were admitted to ICU with acute kidney injury (AKI), in Saudi German Hospital-Jeddah, Saudi Arabia, from 2013 to 2016, and received treatment by CRRT.

Inclusion criteria

Adult patients (Age>18 years) were admitted to ICU, either due to medical or surgical cause with AKI.

Patients were categorized into two groups according to stage of AKI according to Kdigo AKI Work Group [3].

Exclusion criteria

Other than those critical ICU patients with AKI, aged less than 18 years, some other patients were excluded from the study, such as those who were diagnosed as rapidly progressive glomerulonephritis (RPGN), small vessel vasculitis, Good Pasture's disease, cryoglobulinemia, lupus nephritis, hemolytic uremic syndrome, thrombotic thrombocytopenic purpura, toxemia of pregnancy, severe drug poisoning and transplant patients.

All patients' data were collected as regard to

I- **Clinical/biochemical parameters at initiation of CRRT** including (age, sex, body mass index, cause of AKI, comorbidities, history of post-operative or cardiac catheterization, sepsis as a cause of ICU admission, use of mechanical ventilation, medications, vassopressor support and ICU stay time).

II- **Laboratory Data** included serum creatinine, blood urea nitrogen, potassium, calcium, magnesium, phosphrous, albumin, arterial blood gases, INR, PT, PTT and CB).

III- **CRRT Data** included duration of CRRT in hours, dialysate flow rate in ml/kg/hr, and time of initiation CRRT from date of ICU admission).

IV – **Measures of clinical outcomes**

Details of patient's charts and data were revised till patients were recovered, maintained on dialysis, died or lost to follow up

- The **primary outcome measure** mortality 60 days.
- **Secondary outcome** kidney recovery and/or dialysis independence, duration of stay in ICU.

RESULTS

This was a retrospective cohort study, included 100 patients who were admitted to intensive care unit, at Saudi German Hospital-Jeddah, in the period between 2013 and 2016. 59 % of patients were males and 41 % were females. 50 % of the total number of patients was treated by early CRRT (the early group) and the other 50 % were treated by late CRRT (the late group). Regarding the outcome data; ICU mortality was 74% for the early group, but 68% for the late one. Recovered AKI was achieved in 26% of the early group, while it was achieved in 30% of the late one. The survival curve revealed no significant difference between both groups of patients regarding the time and percentage of survival.

So the results of our study revealed no significant differences regarding the outcome between both groups of patients. ICU mortality was even slightly higher in the early group (74 % versus 68 %). Also recovered AKI was slightly lower in the early group (26 % versus 30 %). These data mean that no beneficial role of early CRRT in critical ICU patients with AKI, in terms of improving the outcome of these patients.

The outcome of the total studied patients was found to differ according to some demographic and laboratory data. Of the demographic data, the mean systolic blood pressure (SBP) was found to be significantly lower in the non-recovered cases than the recovered ones (113 versus 121), the associated co morbidities of DM, malignancy, surgery, chronic obstructive pulmonary disease (COPD), ischemic heart disease (IHD) and congestive heart failure (CHF) were all found to be insignificantly higher in the non-recovered cases while hypertension (HTN) was insignificantly higher in the recovered ones. Of the laboratory data, serum magnesium and albumin were significantly lower in the non-recovered cases while WBCs, PTT and INR were significantly lower in the recovered ones.

DISCUSSION

From the above mentioned data and results of the statistics, it was apparent that the group of patients selected for early CRRT was somewhat more critical than those selected for late CRRT, as a higher proportion of them had low systolic BP and/ or having serious associated comorbidities. So, there was 8% higher mortality in this group, despite early CRRT. Conversely, the group of patients selected for late CRRT, were less critical and having a better cardiac and/or pulmonary functional reserves, at least allowing them to be presented late, so there was a slightly better outcome in this group, despite late CRRT. This means that the outcome of patients with AKI, especially those in ICU, depends largely on several other factors rather than the timing of initiation of CRRT. These factors include the cause of ICU admission, associated comorbidities, some serious laboratory variables.. etc. For patients with AKI associated with terminal medical and/or surgical disease as those of malignancy. Early CRRT in those

patients, might be associated with serious inherent complications related to the procedure itself, even more than these reported in other non-terminal patients.

The results of our study were against the results of many studies that reported improved outcome with early CRRT in critical ICU patients with AKI. These studies include (PICARD study) [4].

However, the results of our study are matched with the results of some other studies such as (AKIKI trial) [11].

Finally, a neutral balance should be reached regarding the risk-benefit ratio of the procedure of early or late CRRT, in each patient. The final decision for early or late CRRT, should be individualized according to the clinical and laboratory parameters of each patient. It should also include the openion of senior nephrologists, experienced in management of AKI. The decision should be sensitively communicated to the patients and/or their relatives, explaining the actual role of CRRT in management of their critical disorder.

REFERENCES

1- **Hoste EA, Bagshaw SM, Bellomo R *et al.*(2015)** Epidemiology of acute kidney injury in critically ill patients the multinational AKI-EPI study. Intensive Care Med., 41(8) 1411-1423.

2- **Jun M, Heerspink HJ, Ninomiya T *et al.*(2010)** Intensities of renal replacement therapy in acute kidney injury a systematic review and meta-analysis. Clin. J. Am. Soc. Nephrol., 5(6)959-963.

3- **KDIGO AKI Work Group(2012)** KDIGO clinical practice guideline for acute kidney injury. Kidney Int., 2 1-13.

4- **Zarbock A, Kellum JA, Schmidt C *et al.*(2016)** Effect of early vs delayed initiation of renal replacement therapy on mortality in critically ill patient with acute kidney injury. JAMA. , 315(20) 2190-2199.

5- **Shingarev R, Wille K and Tolwani A(2011)** Management of complications in renal replacement therapy. Semin. Dial., 24 164-168.

6- **Jamale TE, Hase NK, Kulkarni M *et al.*(2013)** Earlier start dialysis in patients with community-acquired acute kidney injury a randomized controlled trial. Am. J. Kidney Dis., 62(6)1116-1121.

7- **Elseviers MM, Lins RL, Van der Niepen P *et al.*(2010)** Renal replacement therapy is an independent risk factor for mortality in critically ill. Patient with acute kidney injury. Crit Care, 14(6)221-229

8- **Payen D, Mateo J, Cavaillon JM *et al.*(2009)** Impact of continuous venovenous hemofiltration on organ failure during the early phase of severe sepsis a randomized controlled trial. Crit. Care Med., 37 803-810.

9- **Pannu N , Noel G *et al.* (2005)** Renal replacement therapy in the intensive care unit Ther. Clin. Risk Manag., 1(2) 141–150.

10- **Bouchard J, Soroko SB, Chertow GM, Himmelfarb J, Ikizler TA, Paganini EP and Mehta RL(2009) Program to improve care in acute renal disease study group.**Kidney Int., 76(4)422-427. doi 10.1038/ki.2009.159.

11- **Gaudry S, Hajage D, Schortgen F *et al.*(2016)** Initiation strategies for Renal-Replacement Therapy in the intensive care unit . N. Engl. J. Med., 375(2)122-133